Remarks

Upon entry of the foregoing amendment, claims 1-15 are pending in the application, with claims 1, 2 and 11 being the independent claims. New claim 15 is added to separate certain embodiments from claim 13.

Support for the amendment to page 4 of the specification is found, *inter alia*, in original claims 13 and 14. Support for the amendment to page 5 of the specification is found, *inter alia*, in original claims 2, 7 and 8.

These changes are believed to introduce no new matter, and their entry is respectfully requested.

The Objection to the Specification

At Office Action page 2, the specification is objected to as not containing proper antecedent basis for the claimed subject matter. Applicants respectfully traverse this objection.

Myo-inositol derivative (claim 2)

Applicants have copied the language of original claim 2 back into the specification - at page 5.

Glucose G (claim 7)

Applicants have copied the language of original claim 7 back into the specification, also on page 5.

Mixture thereof (claim 8)

Applicants have copied the language of original claim 8 back into the specification, also on page 5.

Cardioangiopathy (claims 13 and 14)

Applicants have copied the language of original claims13 and 14 back into the specification, at page 4.

Summary of the objections to the specification

Accordingly, the specification now provides proper antecedent basis for the terms that were used in the claims and this objection can be withdrawn.

The Objection to Claims 1 and 2

At Office Action page 2, claims 1 and 2 have been objected to because they do not contain a period. Applicants thank the Examiner for noting this. Claim 1 has been canceled and claim 2 has been amended to include a period. Accordingly, this objection can be withdrawn.

Rejections under 35 U.S.C. § 112, second paragraph

At Office Action paragraphs numbers 5-9, claims 10 and 12 are rejected under 35 U.S.C. § 112, second paragraph, for indefiniteness. Applicants respectfully traverse this rejection.

Claim 10 has been canceled. Accordingly, those rejections are moot.

Claim 12 is rejected for use of the phrase "very low." Applicants have amended claim 12 to remove this language.

Accordingly, the rejections under 35 U.S.C. § 112, second paragraph, for indefiniteness can be withdrawn.

Rejection under 35 U.S.C. § 102(b)

At Office Action paragraph number 10, claim 1 is rejected under 35 U.S.C. § 102(b) as being anticipated by Dittrich *et al., Phytochemistry 11*: 245-250 (1971) (herein "Dittrich"). Applicants respectfully traverse this rejection. However, in the interests of advancing prosecution, claim 1 has been canceled. Accordingly, this rejection can be withdrawn.

The First Rejection under 35 U.S.C. § 103

At Office Action paragraphs number 15, claims 1-8 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Dittrich in view of Sultana *et al., Phytochemistry 50*:1249-1253 (1999) or Page (US 6,002,025). Dittrich is relied on as teaching that the compound 5-O-methyl-myo-inositol (sequoyitol) is found in the Taxaceae class and

family of plants. However, the Examminer states that Dittrich does not teach a method of extracting the compound from the plants.

The Examiner states that the steps and solvents disclosed in claims 2-8 are well known and are taught by Sultana and by Pagé. The Examiner states that one of ordinary skill in the art at the time the invention was made would have found it obvious to extract the compound sequoyitol from the Taxaceae class and family of plants as disclosed in Dittrich by using well known steps and solvents such a those taught by Sultana and Pagé. Applicants respectfully traverse this rejection.

Claim 1 has been canceled. The methods as claimed in claims 2-8 are a process for extracting 5-O-methyl-*myo*-inositol from Taxus spp. Independent claim 2 has been amended to recite that the extractum is subjected to a diphase extraction and a chromatography using macroporous resin column. Additionally, the specific organic solvent used for extraction and the solvent used for diphase extraction are now also recited.

The process of the present invention uses macroporous resin chromatography as the key step for isolation and purification of sequoyitol. The process of the invention is optimized with regard to large scale use. With regard to claim 3, the applicant selected the two species of Taxus, Taxus yunnanensis and Taxus chinensis var. mairei, the listed sources of plant material, due to their high sequoyitol content and very low pinitol content and this also contributes to that aspect of the claimed method of sequoyitol's extraction and purification.

Moreover, as the conditions of the process are optimized, the isolation yield of sequoyitol in the process of the present invention is up to around 0.1%. But, the procedures of the cited art for sequoyitol's isolation were in a much small scale, in amounts only for laboratory assay, and the procedures were not optimized.

For example, Dittrich only reported the isolation of a very small amount of D-1-O-methyl- muco- inositol from the needles of *Juniperus communis* by paper chromatography and the identification assay for sequoyitol. This article only reports the brief identification assay for sequoyitol. It does not suggest any isolation or purification procedure for sequotyitol, much less one that is useful for large scale use.

Sultana used Melicope micrococca as plant material. The yield of sequoyitol was very low, and the amount of isolated sequoyitol was very small (only 18 mg). The isolation and purification procedure was not optimized. The purity data for isolated sequotyitol was not reported. In Sultana, 242g of Melicope micrococca (Rutaceae) was extracted in a Soxhlet separately and successively with petroleum ether, EtOAc and MeOH. Extracts were concentrated. 11.63g of the EtOAc extract was fractionated by VLC. The VLC fraction eluted with 15-20% MeOH in EtOAc was purified by CC over silica gel to give sequoyitol (18mg only).

Pagé discusses various extraction procedures for paclitaxel and other taxanes that had previously been used in the art. There is no suggestion that the processes discussed in Pagé would lead to the process claimed herein or that the process of the instant methods would provide a process for extracting sequoyitol that resulted in better yields and was amenable for large scale use, both advantages that flow from the invention.

Thus, neither Sultana nor Pagé cure the deficiencies of Dittrich. The examiner states that certain steps and solvents disclosed in claims 2-8 are well known and are taught by Sultana and by Pagé. However, the mere fact that certain extraction steps and solvents were known and used by others for extraction of other materials does not render the current claims as a whole obvious. It is not necessary to invent new solvents or completely new methodologies to impart patentability to a claimed process. Instead the process must be looked at as a whole. Applicants respectfully submit that when their claims process is looked at as a whole, the combination of the cited art does not detract from the non-obviousness of the invention.

The arguments above demonstrate that the claimed method is not suggested by the combination of the cited art. Accordingly, *prima facie* obviousness is not established and this rejection can be withdrawn.

The Second Rejection under 35 U.S.C. § 103

At Office Action paragraphs number 16, claims 1 and -14 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Ostlund (US 5,550,166) in view of Dittrich. Ostlund is relied on as teaching the compound pinitol, compositions containing pinitol and its use in the treatment of diabetes. Dittrich is relied on as teaching that pinitol is a stereoisomer of sequoyitol. The Examiner states that one of ordinary skill in the art at the time the invention was made would have found it obvious to utilize seuoyitol in a composition for the treatment of diabetes as taught by Ostlund, because compounds that

are similar in structure are expected to have similar properties. Applicants respectfully traverse this rejection.

The stereochemical structures of inositol are very complicated. There are several chiral carbons in inositols. Inositols include myo-inositol, chiro-inositol, neo-inositol, scyllo-inositol, epi-inositol (see G. P. Moss, Nomenclature of Cyclitols, Recommendations, 1973. (see, **EXHIBIT 1**, Nomenclature of Cyclitols, Recommendations, 1973, http://www.chem.qmul.ac.uk/iupac/cyclitol/).

Sequoyitol belongs to the myo-inositols and it is 5-O-methyl-myo-inositol. Pinitol belongs to chiro-inositols and it is 3-O-methyl-chiro-inositol. Therefore, sequoyitol and pinitol are different compounds with different stereochemical structures.

It is well known in the art that the activities of chiral active compounds are closely related to their stereochemical structures. For example, the azole nucleoside of D-pinitol is an azole nucleoside analogue of D-pinitol, but it acts as a potential antitumor agent (See **EXHIBIT 2**). Myo-inositol is a parent compound of sequoyitol, but it acts as a lipotropic agent like the Vitamin B complex (See **EXHIBIT 3**). Inositol hexanicotinate is also a derivative of myo-inositol, but its activity is to reduce lipaemia (See **EXHIBIT** 4: Science Direct - Biochemical Pharmacology Effects). That is to say, although the structures of these compounds are very similar, the activities that they have are very different. Therefore, the mere fact that pinitol is a stereoisomer of sequoyitol does not create a presumption that if one is useful to treat diabetes the other will be too.

Dittrich does not cure the deficiencies of Ostlund. Dittrich is silent with regard to whether pinitol and sequoyitol would share this characteristic. The combination of

Dittrich and Ostlund does not reach the claimed invention, and does not render it *prima facie* obvious. Accordingly, this rejection can be withdrawn.

Conclusion

Prompt and favorable consideration of this amendment and reply is respectfully requested. Applicants believe the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided, or to send an e-mail at the e-mail address provided.

Respectfully submitted,

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